REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

The specification has been amended herein to replace "allergic rhinitis (rhinoconjunctivitis)" with "allergic rhinitis or rhinoconjunctivitis". Basis for these amendments, made to further clarify that allergic rhinitis is a different condition from rhinoconjunctivitis, may be found at page 1, lines 17-18 and 34-36 of the specification. Page 1, lines 17-18 of the specification define rhinoconjunctivitis as "hay fever combined with an *ocular symptomatology*" [emphasis added]. The concrete symptoms of rhinoconjunctivitis are described on page 1, lines 34-36 as "itching, reddening, swelling, rhinorrhea and lacrimation". In contrast to rhinoconjunctivitis, allergic rhinitis does not show the ocular symptoms.

Claims 2, 3, 5, 6, 9 and 11 are amended herein. Basis for these amendments may be found throughout the specification and claims as-filed especially at page 4, lines 24-33. Thus, no prohibited new matter is presented by way of the present Amendment. Applicants reserve the right to file a continuation or divisional application directed to any subject matter deleted by way of this Amendment.

Objections to the Specification

The specification is objected to under 37 C.F.R. § 1.71 because it is purportedly unclear if allergic rhinitis is a condition distinct from rhinoconjunctivitis.

To clarify that allergic rhinitis and rhinoconjunctivitis are not the same condition, Applicants have amended the specification by way of the present Amendment, to replace "allergic rhinitis (rhinoconjunctivitis)" with "allergic rhinitis or rhinoconjunctivitis". This amendment is made to attend to issues of English grammar, in order further clarify that these two conditions as separate conditions. Applicants note that the specification as-filed, on page 1, recites "rhinoconjunctivitis (hay fever combined with an ocular symptomatology)". The symptoms of rhinoconjunctivitis are listed as "the acute symptoms (itching, reddening, swelling, rhinorrhea and lacrimation". Thus, rhinoconjunctivitis is distinguished in that it displays ocular symptoms. In contrast allergic rhinitis does not show the ocular symptoms exhibited by rhinoconjunctivitis. Allergic rhinitis and rhinoconjunctivitis are two separate conditions. Applicants request that this objection be withdrawn.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-9 and 11 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly failing to comply with the written description requirement. The Office Action indicates that while the specification discloses that the claimed composition and method are intended for local treatment, the broad claims do not recite local treatment. The Office

Action further notes that page 4 of the specification discloses that "topically" means intranasally or intraocularly. Without ceding to the rejections, Applicants have amended the claims herein to recite "intranasally, intraocularly and inhalative", to clarify the methods of administration, as recited in the specification.

Claims 5-9 and 11 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while enabling for a method of treating rhinoconjunctivitis, purportedly does not provide enablement for all disorders of the lower and upper airway or for the treatment of all allergies. Without ceding to the rejection, Applicants have amended claims 5 and 9 to recite "A method for the treatment of allergic disorders of the lower or upper airways and the eyes comprising..." and "A method for the treatment and prophylaxis of allergic airway and eye disorders, comprising..." respectively.

Applicants further note that the fact that allergic diseases of the nose, eyes and upper or lower airways (including asthma) may be treated with loteprednol/antihistamine is described by the examples in the instant specification. The significant reduction of nasal symptoms of these diseases is described on page 6 (providing a discussion of the overadditive effect of the claimed combination for the reduction of nasal secretion). The example on page 6 shows a more general effect with the inhibition of TNFα release. TNFα has long been considered to be an important proinflammatory cytokine that is generally involved in allergic inflammatory processes. A typical sign for such an inflammatory process is an increase in TNFα release. It is known in the art that these

inflammatory processes underlie all allergic reactions the conclusion from the example is that the claimed combination is a suitable and effective treatment for all allergic diseases of nose, eye, upper or lower airways, including asthma bronchiale.

Thus, Applicants submit that in light of the amendments to the claims, as well as what is recited in the specification and known in the art, the claims are enabled and supported with adequate written description. Applicants request that the rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-9 and 11 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Claims 1, 4, 9 and 11 stand rejected, as the phrase "pharmaceutically tolerable ester" is purportedly colloquial. The claims have been amended to recite "pharmaceutically acceptable ester". Claims 3, 5 and 9 stand rejected, as the phrase "and/or" is purportedly confusing. The claims have been amended to recite only "or".

Claims 6 and 9 stand rejected, as it is purportedly unclear if the patient is required to have more than one disorder. Applicants submit that based on the amendments made herein clarifying the disorders at issue, as well as in light of the specification, the skilled artisan would understand that the claimed methods may treat and/or prevent the disorders at issue. Applicants submit that the specification and claims do not require that the patient have more than one disorder at one time.

Claims 6-8 stand rejected, as it is purportedly unclear as to whether loteprednol and the antihistamine are administered simultaneously, sequentially, separately or independently of one another. The claims have been amended herein to recite that the administration may take place simultaneously, sequentially or separately, as indicated in the specification. Claims 7 and 8 stand rejected, as they purportedly do not further limit claim 5 from which they depend. The claims have been amended to recite that the administration is intranasally, intraocularly and inhalative. Claim 6 is also amended herein to replace "such" with "said", for clarification.

Claims 5 and 9 stand rejected, as it is purportedly unclear as to how treatment of allergies distinguishes over disorders of the lower and upper airways. The claims have been amended to remove "and/or for the treatment of allergies". Claim 9 stands rejected, as it is purportedly unclear as to how the loteprednol and the antihistamine(s) are mixed "individually". Claim 9 has been amended to remove "individually". Claim 11 stands rejected, as is purportedly confusing as to whether two distinct conditions are claimed. Applicants note that as discussed above, the specification has been amended to clarify that two distinct conditions are claims, each having symptoms distinct from the other.

Thus, Applicants request that these rejections be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 1-9 and 11 stand rejected under 35 U.S.C. § 103 (a) as purportedly unpatentable over Friedlaender. Friedlaender purportedly discloses that antihistamines,

including levocabastine, azelastine and other antihistamines, are used as topically therapy for allergic conjunctivitis. Friedlaender also purportedly discloses that corticosteroid eyedrops, including loteprednol etabonate, are used to treat allergic conjunctivitis. The Office Action notes that the instant composition and method differ over Friedlaender in claiming a composition comprising both loteprednol and an antihistamine and a method in which the loteprednol are administered simultaneously, sequentially or separately. However, the Office Action states that it would be obvious to one of ordinary skill in the art to combine loteprednol and an antihistamine. Applicants traverse.

In order to establish a case of *prima facie* obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See* M.P.E.P. §2142. Applicants respectfully submit that these criteria have not been met in the present Office Action.

Friedlander discloses the antihistamines for the treatment of allergic conjunctivitis, as well as the use of corticosteroid eyedrops to treat allergic conjunctivitis. However, the cited reference fails to disclose or suggest the combination of the two substances as claimed in the instant invention. Applicants submit that the present invention does not just display a simple additive effect. Rather, the specification sets forth clear results showing that there is an unexpected effect in the combination of both substances. Tables 1 and 2 of the specification (pages 5-6) show a highly significant overadditive effect in the combination of

loteprednol and azelastine *in vitro* as well as *in vivo*. Thus, there is not motivation to combine the two substances to achieve the unexpected result of the present invention.

Claims 1-9 and 11 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over EP 709 099 in view of WO 97/01377. '099 purportedly discloses that loteprednol etabonate is used in the treatment of allergic rhinitis.

European Patent No. 0 709 099 discloses aqueous nasal suspensions of hardly soluble drugs with an example of loteprednol. However, the focus of the present invention is on the improvement of pharmacological efficacy by optimizing the pharmaceutical presentation. The cited reference does not contain any hint for medical uses, or any examples or descriptions of the combination of loteprednol with antihistamines. Even in combination with the other cited reference, the cited reference fail to render the claimed invention unpatentable, as the secondary reference fails to remedy the deficiencies of the primary reference.

Applicants note that WO 97/01377 discloses a nasal spray for the treatment of allergic rhinitis containing a combination of levocarbastine or azelastine together with a topical nasal steroid. However, the group of substances from which the reference states the steroid should be selected does not contain loteprednol, nor does the reference contain any data which would support the effectiveness or provide a motivation for the combination of the two substances. In contrast to the cited reference, the present invention displays an unexpected effect from the combination of both substances. The cited reference does not

teach or even suggest this unexpected, overadditive effect. Moreover, Applicants note that not all of the topical steroids listed in the cited reference belong to the group of "soft steroids", as used in the present invention. Thus, there is no motivation for the skilled artisan to pick out the two particular substances of the present invention and expect the same effect upon combination as that seen with the present invention.

Applicants request that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. 02-4800.

Respectfully submitted,

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